III. REMARKS

A. Status of the Claims

Claims 1-13 were originally filed with the case on June 26, 2003. Claims 1, 5, 9 and 13 were amended and claims 14-18 were added in a Preliminary Amendment filed on October 16, 2003. All pending claims were rejected in an Office Action mailed on September 27, 2004. Claims 1, 4, 5, 8, 9, 11, 14, and 16 were amended and claims 3, 7, 11, and 15 were canceled in a Response to Office Action filed on January 27, 2005. All pending claims are rejected in a Final Office Action, mailed on July 14, 2005. Claim 1 is amended herein to correct a typographical error in the claim. No claims are added or cancelled herein.

B. The Claims are Patentable over Penn and Yaacobi

The Action maintains the rejection of all pending claims under § 103(a) as being unpatentable over Penn *et al.* and Yaacobi. The Action asserts that Penn teaches the use of anecortave acetate in a pharmaceutical formulation for the inhibition of angiogenesis of ocular conditions such as macular degeneration. The Action acknowledges that Penn lacks a teaching of the prevention of loss of vision associated with AMD, maintaining visual acuity associated with AMD, the inhibition of lesion growth and the inhibition of blood vessel growth associated with AMD (*i.e.*, the uses claimed in the pending claims). Nevertheless, the Action states that it would have been obvious to use the claimed compound for the claimed uses in light of Penn's teaching of the treatment of macular degeneration. Yaacobi is said to teach the use of a device, which can be implanted into the eye for drug delivery purposes and to mention the use of anecortave acetate in the device. With respect to Applicants' previous arguments, the Action states that the determination of optimum proportions or amounts and

route of administration is considered to be within the skill of the artisan. Applicants respectfully traverse.

The Action asserts that maintaining visual acuity associated with macular degeneration, inhibiting blood vessel growth associated with macular degeneration and inhibiting lesion growth associated with macular degeneration would be inherent properties of a composition known for treating macular degeneration. Applicants submit a publication by The Anecortave Acetate Clinical Study Group, published in RETINA, ("the RETINA article;" attached as Exhibit A), which provides evidence to establish the unexpected or unobvious nature of the claimed invention. The RETINA article reports an interim analysis of the data from the first six months of a study designed to compare the clinical efficacy of anecortave acetate versus placebo treatment for preservation (maintenance) of vision and inhibition of CNV lesion growth. These parameters had not been previously studied.

The results indicate that anecortave acetate 15 mg was statistically superior to placebo treatment at month 6 with respect to mean change in logMAR visual acuity, and that treatment with both anecortave acetate 30 mg and 3 mg was favored over placebo treatment (See Fig. 1, page 18). Furthermore, with respect to the preservation of vision in the large subgroup of patients with a predominantly classic CNV lesion, anecortave acetate 15 mg was significantly better than placebo (See Fig. 3, page 19). This superior efficacy for anecortave acetate 15 mg is further supported by data comparing clinically significant vision loss and severe vision loss (See Table 3 and Table 4, respectively, page 17 and page 19). Additionally, anecortave acetate 15 mg was shown to be statistically superior to placebo treatment for inhibition of total lesion surface area, total CNV surface area, and total classic CNV surface area at month 6 (See Fig. 5, page 21). A trend favoring the anecortave acetate

30 mg and 3 mg treatment regimens over placebo treatment for the inhibition of lesion growth was also observed.

The Action asserts that "animal models are routinely used as preliminary study models for human use," reasoning that the determination of optimum proportions or amounts and route of administration is within the skill of the artisan. Applicants submit that, while animal models are routinely use as preliminary study models, their use typically provides evidence of utility or effectiveness of a compound for a particular disease state represented in the animal model. Once a compounds potential effectiveness is shown in animal models, the task of determining the optimal dosage type, amount and frequency is undertaken. It is well settled patent law that "obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art." *See In re Fine*, 837 F.2d 1071, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 U.S.P.Q.2d 1941 (Fed. Cir. 1992); MPEP § 2143.01.

Furthermore, the fact that a reference or references can be combined or modified is not sufficient to establish obviousness. For example, the Federal Circuit held in *In re Mills*, 916 F.2d 680, 16 U.S.P.Q.2d 1430 (Fed. Cir. 1990), that the mere fact that combination or modification of a reference or references is possible does not establish obviousness of the resultant combination unless the prior art also suggests the desirability of the combination, *i.e.*, unless the prior art provides motivation to produce the resultant combination or make the resultant modification. *Mills*, 16 U.S.P.Q.2d at 1432; *see also* MPEP § 2143.01, page 2100-91.

Moreover, the Board of Patent Appeals and Interferences has held that the fact that the claimed invention is within the capabilities of one of ordinary skill in the art is not sufficient by itself to establish obviousness. *Ex parte Levengood*, 28 U.S.P.Q.2d 1300 (BPAI 1993). Section 2143.01 of the MPEP explains the *Levengood* holding as follows:

> A statement that modifications of the prior art to meet the claimed invention would have been "'well within the ordinary skill of the art at the time the claimed invention was made'" because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings of the references.

MPEP § 2143.01, page 2100-91 (emphasis in original).

Applicants submit that the Action merely states that the modification to the cited art would have been within the ordinary skill of the art without providing the requisite evidence of motivation for the modification. Thus, it is believed that, in light of the unexpected findings of the superiority of the 15 mg dosage and the trend for preference for the 3 mg and 30 mg doses over placebo, and the absence of evidence of motivation for modification of the cited art, the present invention is not obvious over Penn and Yaacobi.

For the foregoing reasons, Applicants respectfully request that the obviousness rejection based on Penn and Yaacobi be withdrawn.

C. Conclusion

Applicants respectfully request that the claims be considered as amended herein.

The Examiner is invited to contact the undersigned attorney at (817) 551-4321 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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